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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Appellants	:	Powell et al.
Serial No.	:	09/303,716
Filed	:	April 30, 1999
For	:	TRANSITION STATE ANALOGS
Group Art Unit	:	1652
Examiner	:	Charles L. Patterson, Jr.

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to:
Asst. Commissioner for Patents
Washington, D.C. 20231, on April 30, 2002

Gerard Bilotto

Signature

4/30/02

Date of Signature

Assistant Commissioner for Patents
Washington, D.C., 20231

Sir:

APPELLANT'S BRIEF ON APPEAL UNDER 37 C.F.R. § 1.192

This is an appeal from the Final Official Action dated May 30, 2001, rejecting claims 36, 39, 42, 45 and 48. Applicants filed a Notice of Appeal on November 30, 2001 under 37 C. F. R § 1.191 and enclosed is a petition for a three (3) months extension of time under provision 37 C.F.R. §1.136(a) is enclosed to extend the time for filing the brief from January 30, 2002 to April 30, 2002.

05/09/2002 [illegible]
02 FC:220

KL3:2175906.1

The instant brief is submitted in triplicate as required by 37 C. F. R. 1.192(a).

A check in the amount of $160.00 is submitted under provision 37 C.F.R §1.17(c) for a small entity.

REAL PARTY IN INTEREST

The real party in interest in this appeal is the assignee, IGEN International, Inc.

RELATED APPEALS AND INTERFERENCES

Appellants are not aware of any related appeals or interferences that directly affect or are directly affected by or have a bearing on the Board's decision in the pending appeal.

STATUS OF CLAIMS

Claims 36, 39, 42, 45 and 48 are pending in the instant application. Claims 1-35, 37-38, 40, 41, 43, 44, 46, 47 and 49 are cancelled.

The claims of this application were rejected in a Final Office Action dated May 30, 2001.

The status of the claims is as follows:

Allowed claims:	None
Claims objected to:	None
Claims rejected:	36, 39, 42, 45 and 48.

These claims are set out in Exhibit A, attached hereto.

The claims on appeal are 36, 39, 42, 45 and 48.

STATUS OF AMENDMENTS

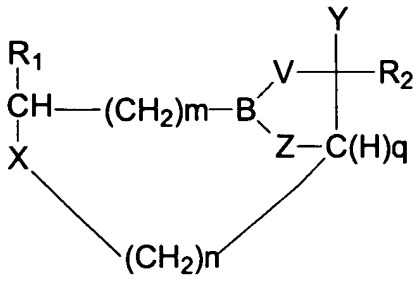
No amendments have been filed subsequent to the final rejection.

SUMMARY OF INVENTION

The present invention broadly relates to compounds (e.g., haptens) which can be used to form antigens capable of eliciting, through immunogenic methods, catalytic antibodies which can catalyze the cleavage or formation of a peptide linkage or an ester bond in a substrate molecule. The catalytic antibodies elicited using the haptens of the invention are capable of recognizing a specific amino acid sequence and selectively proteolyzing a peptide linkage within that sequence. For example, the invention includes catalytic antibodies having an epitope that binds to and thereby stabilizes a tetrahedral carbon transition state in the cleavage or formation of a peptide linkage or an ester bond so that the cleavage or formation is catalyzed by the antibodies. (specifications, page 18, lines 4-27).

The haptens of the invention have been rationally designed from knowledge of the mechanistic features of enzyme catalysis and provide suitable templates for generating antibody combining sites endowed with catalytic properties. The immunogen design provides the binding energy for exerting a strain and/or distortion of the substrate. This energy shifts the substrate from a stable ground-state towards an energetically unfavorable transition-state where proteolysis occurs.

Accordingly, the invention is directed to the boron-containing haptens of the following formula (I) (See Preliminary Amendment filed April 30, 1999 pages 2-3):



(I)

wherein

R_1 and R_2 may be the same or different and each is a side chain of a naturally occurring amino acid, a hydroxy containing side chain of a naturally occurring amino acid wherein said hydroxy group may be glycosylated, phosphorylated, sulphonylated or protected by a hydroxy protecting group, a primary amido containing side chain of a naturally occurring amino acid wherein said amido group may be glycosylated, $(C_2–C_4)$ alkyl, $–CH_2CH(CO_2H)_2$, $–(CH_2)_2 S(O)CH_3$, $–(CH_2)_2 S(O)_2 CH_3$, $–(CH_2)_3 NH_2$ or $–(CH_2)_3 ONHC(=NH)NH_2$;

V is O, CH_2 or NH;

X is hydrogen, oxygen, amino, amino protected by a terminal amino protecting group, amino bonded to the C terminus of a naturally occurring amino acid to form a peptide bond, amino bonded to the C terminus of a peptide to form a peptide bond, alkene, $(C_1–C_9)$alkyl, $(C_1–C_9)$ alkoxy or phenyl, phenoxy, cyclohexyl, phenylthio, phenylsulfinyl or phenylsulfonyl, wherein the aforementioned phenyl groups may be unsubstituted or mono-, di- or trisubstituted by halogen, $(C_1–C_4)$alkoxy or (C_1-C_4)alkoxycarbonyl;

Y is hydrogen, carboxyl, carboxyl protected by a terminal carboxyl protecting group, a carbonyl bonded to the N terminus of a peptide through a peptide bond, $(C_1–C_9)$alkyl, $(C_1–C_9)$alkoxy, phenyl phenoxy, cyclohexyl, phenylthio, phenylsulfinyl or phenylsulfonyl wherein the aforementioned phenyl groups may be unsubstituted or mono-, di- or trisubstituted by halogen, $(C_1–C_4)$alkyl, (C_1-C_4)alkoxy or (C_1-C_4)alkoxycarbonyl; and wherein

Z is O, CH_2 or NH;

m is 0 or an integer from 1 to 10;

n is 0 or 1; and

q is 1 or 2 provided that if q is 2, then n=0 and there is no bond between X and the carbon bound to Z.

The haptens of the instant invention can be used as antigens for eliciting catalytic antibodies by combining the hapten with a suitable carrier molecule.

Another aspect of the invention is directed to catalytic antibodies which are elicited by antigens comprising the haptens of the invention. Similarly, the invention is also directed to catalytic antibodies which can catalyze a chemical reaction of interest and which are elicited through in vitro or in vivo techniques by antigens comprising the haptens of the instant invention.

Another aspect of the invention is directed to a method for producing catalytic antibodies which can catalyze a chemical reaction of interest and which are elicited through in vitro or in vivo techniques by antigens comprising the haptens described above. The method comprises of 1) exposing cells capable of producing antibodies to the antigens and thereby generating antibody producing cells; 2) hybridizing the antibody producing cells with myeloma cells thereby generating a plurality of hybridoma cells each producing monoclonal antibodies; and 3) screening the plurality of monoclonal antibodies to identify a monoclonal antibody which catalyzes the chemical reaction of interest.

The invention is also directed to a method for catalyzing the cleavage or formation of a peptide linkage in a molecule. The method comprises contacting the molecule with an effective amount of a catalytic antibody which has been elicited by antigens comprising haptens according to the invention.

Several specific embodiments of the invention are described in the specification. These include:

- A methodology for the synthesis of (S)-lactate-1-(R)-amino-2-phenylethane boronate, a preferred boron-containing hapten of formula I, is shown in FIG. 15. (Example 3, specification Page 67, line 4 to page 68, line 26).
- A methodology for producing and isolating monoclonal antibodies which can catalyze a chemical reaction of interest and which are elicited through in vitro or in vivo techniques by an antigen. The antigen comprises a hapten according to the invention. (Example 6, specification Page 75, line 1 to page 81, line 22).

ISSUES

Whether the subject matter of claims 36, 39, 42, 45 and 48 was described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention under 35 U.S.C. § 112, first paragraph.

GROUPING OF CLAIMS

It is Appellants' contention that claims 36, 39, 42, 45 and 48 stand or fall together.

ARGUMENT

Claims 36, 39, 42, 45 and 48 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly not being described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

It is unclear what is the basis for this rejection as the specification clearly provides support for the claimed subject matter in compliance with the "written description" and enablement requirements under 35 USC § 112, first paragraph.

The "enablement" and "written description" requirements under 35 U.S.C. §112, first paragraph, are separate and distinct. See, MPEP Section 2161. It appears that the Examiner is confusing the "written description" and the "enablement" requirements of 35 U.S.C. § 112, first paragraph.

The written description requirement of 35 U.S.C. § 112, first paragraph specifies that the invention need not be described in such a "...full, clean, concise, and exact terms as to enable any person skilled in the art...to make and use the same...". The subject matter of the claimed invention need not be described literally or in *ipsis verbis* for the specification to satisfy the description requirement. *In re Lukach*, 442, F.2d 967, 969 (C.C. P.A. 1971), *Martin v. Johnson*, 454 F.2d 746, 751, 172 U.S.P.Q. 391, 395 (C.C.P.A. 1972). Further, it is sufficient that the specification convey to those skilled in the art the fact that the applicant invented the claim subject matter. *In re Wertheim*, 541 F.2d 257, 262 (C.C.P.A. 1976).

The written description requirement of 35 U.S.C. § 112, first paragraph ensures that a patent is granted to inventors who had possession, as of the filing date of the application relied on, of the specific subject matter later claimed by them. How the specification accomplishes this is immaterial. *In re Smith*, 178 U.S.P.Q. 620 (C.C.P.A. 1973). *In re Kaslow*, 217 U.S.P.Q. 1089 (Fed. Cir. 1983). (See also, MPEP, Section 2163.02).

The Examiner asserts "...that the experimentation required to practice the claimed invention would be undue given the broad category of hapten shown in the instant claims and the fact that there is not one example given where a catalytic antibody has been made using any of these wide ranging possible haptens" (Final Official Action dated May 30, 2001, page 3). Contrary to Examiner's assertion, the specification provides an extensive disclosure of the claimed compounds and a detailed description of the various synthetic methods for preparing

such compounds (specification, Example 3, page 67, line 4 to page 68, line 26). "In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus" (*Reagents of the University of California v. Eli Lily*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997); (See also MPEP 2163).

One of ordinary skill in the art would readily recognize from the original disclosure that Appellants invented the presently claimed subject matter. The Examiner's allegation that the specification is deficient in that it does not show an "example ... where a catalytic antibody has been made" (Final Official Action dated May 30, 2001, page 3, lines 3-4) is not relevant to a determination of whether Appellants' have satisfied the written description requirement under 35 USC § 112, first paragraph. Therefore, Appellants request that this rejection be reversed.

Appellants believe the Examiner is confusing the "enablement" and "written description" requirements under 35 U.S.C. § 112, first paragraph. Accordingly, Appellants provide the following arguments to overcome implicit enablement rejection.

Appellants respectfully submit that the presently claimed subject matter is enabled by the specification in compliance with the first paragraph of 35 USC § 112. The "enablement" requirement under 35 U.S.C. §112, first paragraph, requires nothing more than objective enablement. Whether this is achieved by illustrative examples or by broad terminology is of no importance. *In re Marzocchi*, 169 U.S.P.Q. 367 (C.C.P.A. 1971). An assertion by the Patent Office that the enabling disclosure is not commensurate with the scope of the protection sought must be supported by evidence or reasoning substantiating the doubt so expressed. *In re Dinh-*

Nguyen, 181 U.S.P.Q. 46 (C.C.P.A. 1974); *In re Bowen*, 181 U.S.P.Q. 48 (C.C.P.A. 1974); *In re Armbruster*, 185 U.S.P.Q. 152 (C.C.P.A. 1975).

It is improper to reject claims on the ground that the specification does not support the claims when the terms of the claim are no broader than the broadest description of the invention in the specification and there is no reason to challenge the operativeness of the subject matter embraced by the claims. *Ex parte Altermatt*, 183 U.S.P.Q. 436 (POBA 1974).

There is no reasonable basis set forth in the Office Action to support the Examiner's assertion that the presently claimed subject matter is not enabled by the present specification. One of ordinary skill in the art would be able to practice the presently claimed subject matter in view of the specification and the prior art without undue experimentation.

In the Final Office Action, the Examiner asserts:

> It is maintained that the experimentation required to practice the claimed invention would be undue given the broad category of hapten shown in the instant claims and the fact that there is not one example given where a catalytic antibody has ever been made using any of these wide ranging possible haptens.

(Final Office Action, page 3).

Contrary to the Examiner's suggestion, the specification need not provide examples or specific description of embodiments for the entire scope of the invention. Detailed procedures for making and using an invention may not be necessary if the description of the invention itself is sufficient to permit those skilled in the art to make and use the invention (MPEP §2164). A patent does not teach, **and preferably omits**, what is well known in the art. *In re Buchner*, 18 U.S.P.Q.2d 1331, 1332 (Fed. Cir. 1991); *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 231 U.S.P.Q. 81, 94 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987); *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 221 U.S.P.Q. 481, 489 (Fed. Cir. 1984). (See also,

MPEP § 2164.01). Compliance with the enablement requirement of 35 U.S.C. § 112, first paragraph, does not turn on whether an example is disclosed or whether an example is working or prophetic in nature (See, MPEP § 2164.02).

To assert a rejection for lack of enablement, the Examiner must meet the initial burden of establishing a reasonable basis to question the enablement provided for the claimed invention. *In re Wright*, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993). See also, MPEP §2164.04. The Examiner has failed to present any evidence or reasoning substantiating the allegation that the presently claimed subject matter is not enabled.

Accordingly, the burden of proving enablement has not shifted to the Appellants and therefore the rejection is improper and should be reversed.

Even assuming *arguendo* that a reasonable basis for objecting to the specification was set forth in the Office Action, the description provided in the specification is sufficient to overcome the objection.

Contrary to Examiner's assertions, the specification provides extensive disclosure of the claimed haptens and the synthetic methods for preparing the claimed compounds (e.g. specification, page 41, lines 11 to 18 and 21, page 42, line 3 to page 53, line 13 and Example 3 page 67, line 4 to page 68, line 26). The specification provides ample guidance to the person of ordinary skill in the art in eliciting catalytic antibodies by the haptens and immunogens of the currently pending claims (specification, page 56, line 4 to page 60, line 21, and Detailed Examples 6-9 Page 75, line 1 to page 89, line 7). Every stage of the process is disclosed in great detail.

Several specific embodiments of the invention are described in the specification. These include:

- A methodology for the synthesis of (S)-lactate-1-(R)-amino-2-phenylethane boronate, a preferred boron-containing hapten of formula I, is shown in FIG. 15. (Example 3 Page 67, line 4 to page 68, line 26)
- A methodology for producing and isolating monoclonal antibodies which can catalyze a chemical reaction of interest and which are elicited through in vitro or in vivo techniques by an antigen was described as an example of an antibody designed to cleave "Flap" region of Human Renin. The antigen comprises a hapten according to the invention and the chemical structure of the hapten is specifically designed to mimic the high-energy transition state of an amide bond. (Example 6 Page 75, line 1 to page 81, line 22)

Thus, the specification discloses how to make the haptens, how to use the haptens to generate catalytic antibodies and how to test the antibodies for the desired activity. The disclosure in the present specification including the examples is sufficient to enable one of ordinary skill in the art to practice the claimed invention without undue experimentation.

In addition, Appellants remind the examiner that working examples are not a requirement for satisfying the first paragraph of 35 U.S.C. 112 (See, MPEP Section 2164.02). Moreover, the test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, is it undue. *In re Angstadt*, 190 USPQ 214, 219 (C.C.P.A. 1976) (MPEP 2164.01).

Furthermore, in addition to the teachings provided in the specification, Appellants have cited references demonstrating the high state of the relevant art (Gao et al.).

The Examiner asserts, "While the [Gao] reference does show that a trigonal boronic hapten will produce a catalytic antibody, the hapten is not the same as that of the instant claims" (Final Office Action, dated May 30, 2001, page 3).

Appellants submit that the differences between the haptens of the instant claims and the haptens of Gao relate to the difference in the reactions they have been selected to catalyze. The claimed haptens are directed towards antibodies that cleave internal amide bonds while the haptens of Gao are directed towards generating antibodies that cleave primary amides. The haptens of Gao are similar to the claimed haptens of the instant invention, because both are created to emulate the high-energy state of amides and are targeting elicitation and selection of antibodies for catalysis of amide hydrolysis.

Appellants submit that the teachings of Gao combined with the extensive disclosure of how to make the haptens (specification, page 49, line 19 to page 55, line 19 and Examples 1-5 pages 63 to 74), how to use the haptens to generate catalytic antibodies and how to select the antibodies for the desired catalytic activity (specification, page 56, line 5 to page 60, line 21 and Examples 6 through 9, pages 75 to 89) provides a strong support for the enablement of the presently claimed subject matter. The teachings of Gao are clearly relevant to the presently claimed subject matter. "Courts have routinely found evidence of structural similarity to a compound known to have a particular therapeutic or pharmacological utility as being supportive of an assertion of therapeutic utility for a new compound" (MPEP 2107.03, Section II).

The Examiner asserts that "The catalytic antibody art is unpredictable and the reference presented, Gao et al. (U), is indicative of this" (Final Office Action, dated May 30, 2001, page 3).

Appellants respectfully traverse the Examiner's statement. In discussing catalytic antibody technology, Gao merely teaches that "while this approach has proven largely successful for over 50 chemical reactions, there are some transformations which have proved resistant to this methodology" (page 2211 first paragraph, lines 7-10). Even assuming, *arguendo*, that some transformations are resistant to catalytic antibody methodology, which is not the case for amide bond hydrolysis when a trigonal boronic hapten is used, it is not necessary for this approach to be successful in every case to satisfy the enablement requirement of 35 USC § 112, first paragraph. As stated in the MPEP:

> The presence of possible inoperative embodiments within the scope of a claim does not necessarily render a claim non-enabled. The standard is whether a skilled person could determine which embodiments that were conceived, but not yet made, would be inoperative or operative **with expenditure of no more effort than is normally required in the art.**

[MPEP 2164.08(b), emphasis added].

Appellants assert that the "fifty successful transformations" taught by Gao is a significant enough number to further demonstrate and establish the enablement of the instant application or at least rebut the Examiner's unsupported assertions of non-enablement. Furthermore, catalytic antibodies that cleave the "Flap" region of Human Renin were disclosed in the specification of the instant invention (specification, Example 6).

The Examiner argues there is support for the assertion relating to the unpredictability of the art of catalytic antibodies in the "paragraph spanning pages 2216-2217 and the next paragraph" of the Gao et al. reference (Final Official Action, dated May 30, 2001, page 3).

Appellants respectfully directed the Examiner's attention to the following citations from Gao et al. including the paragraph spanning pages 2216-2217 and the following paragraph (page 2217) which further demonstrate that the presently claimed invention is fully enabled. More

specifically, the following statements demonstrate a successful example of using a boron-containing hapten to elicit catalytic antibodies and the high reproducibility of the disclosed methodology:

> "The observed rate enhancement supplied by BL25 reduced the half-life of the primary amide in **1a** from ca. 17.5 years to 3.9 h in the presence of the catalytic Fab and is >2 orders of magnitude higher than that observed for an antibody elicited by a phosphinate transition-state analog approach, highlighting the power of this direct selection strategy with the boronic hapten probe." (pp. 2216-2217)

> "Finally, equally active protein was purified from three different fermentation batches." (p. 2217)

Therefore, Appellants submit that Gao et al. provides additional evidence of the level of skill in the art and the enablement of the present claims. Moreover, the following publication was submitted by Appellents to further demonstrate the general knowledge in the art:

> Nevinsky GA, Semenov DV, Buneva VN.
> *Catalytic antibodies (Abzymes) Induced by Stable Transition-State Analogs*
> Biochemistry (Moscow) 2000; 65(11): 1233-44.

The reference includes twenty-four examples compiled in a comprehensive table format of successful catalytic antibody productions where transition-state analogs were employed. This review demonstrates the level of skill in the art and provides further evidence that the presently claimed subject matter is fully enabled to one of ordinary skill in the art.

The test for enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. *In re Angstadt*, 190 U.S.P.Q. 214 (CCPA 1976). See also, MPEP § 2164.01. The fact that experimentation may be complex does not necessarily make it undue if those skilled in the art typically engage in such experimentation. *In re Certain Limited - Charge Cell Culture Microcarriers*, 221 U.S.P.Q. 1165, 1174 (Int'l Trade Comm'n

1983); *M.I.T. v. A.B. Fortia*, 227 U.S.P.Q. 428 (Fed. Cir. 1985); *In re Wands*, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988). See also, MPEP § 2164.01.

In the instant invention the experimentation is not undue because a person of ordinary skill in the art regularly engages in this type of experimentation as evidenced by the large number of references in the review cited above.

The art of catalytic and non-catalytic monoclonal antibodies inherently involves some experimentation. The process requires immunizing an animal with a variety of haptens, removing spleen cell, hybridizing spleen cells with myeloma cells to produce immortalized hybridoma cells and screening hybridoma cells to identify cells producing monoclonal antibodies with the desired properties. The protocol is conventional in the art and specific adaptation of the protocol to produce catalytic antibodies of the present invention is disclosed in the specification (page 56, line 5 to page 60, line 21) in great detail. Applying such protocol to practice the claimed invention does not require undue experimentation.

As clearly stated in the MPEP:

> (B) In *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988), the court reversed the rejection for lack of enablement under 35 U.S.C. 112, first paragraph, concluding that undue experimentation would not be required to practice the invention. The nature of monoclonal antibody technology is such that experiments first involve the entire attempt to make monoclonal hybridomas to determine which ones secrete antibody with the desired characteristics. The court found that the specification provided considerable direction and guidance on how to practice the claimed invention and presented working examples, that all of the methods needed to practice the invention were well known, and that there was a high level of skill in the art at the time the application was filed. Furthermore, the applicant carried out the entire procedure for making a monoclonal antibody against HBsAg three times and each time was successful in producing at least one antibody which fell within the scope of the claims.

[MPEP 2164.06(b)]

Appellants assert that one of ordinary skill in the art could practice the presently claimed invention without undue experimentation.

Therefore, there is no reasonable basis set forth in the Final Office Action, dated May 30, 2001 to support the Examiner's assertion that the presently claimed subject matter is not enabled by the present specification.

Hence, Appellants respectfully submit that the presently claimed subject matter is fully enabling to one of ordinary skill in the art and described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Therefore, the rejection of the claims under 35 USC § 112, first paragraph, is improper and should be reversed.

Favorable reconsideration and withdrawal of the Section 112, first paragraph rejection are earnestly solicited.

CONCLUSION

In view of the foregoing, Appellants respectfully submit that the instant claims are described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Therefore, the rejection of the claims should be reversed and the claims allowed. Such action is earnestly solicited.

Respectfully submitted,

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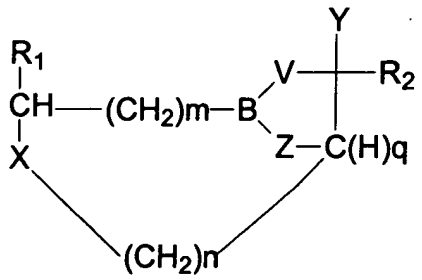
EXHIBIT A

PENDING CLAIMS AS AUGUST 27, 2001

CLAIMS 36, 39, 42, 45, 46 and 48

36. A catalytic antibody elicited by an antigen comprising the boron-containing hapten of formula I,



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wherein

R_1 and R_2 may be the same or different and each is a side chain of a naturally occurring amino acid, a hydroxy containing side chain of a naturally occurring amino acid wherein said hydroxy group may be glycosylated, phosphorylated, sulphonylated or protected by a hydroxy protecting group, a primary amido containing side chain of a naturally occurring amino acid wherein said amido group may be glycosylated, (C_2–C_4) alkyl, $-CH_2CH(CO_2H)_2$, $-(CH_2)_2\ S(O)CH_3$, $-(CH_2)_2\ S(O)_2\ CH_3$, $-(CH_2)_3\ NH_2$ or $-(CH_2)_3\ ONHC(=NH)NH_2$;

V is O, CH_2 or NH;

X is hydrogen, oxygen, amino, amino protected by a terminal amino protecting group, amino bonded to the C terminus of a naturally occurring amino acid to form a peptide bond, amino bonded to the C terminus of a peptide to form a peptide bond, alkene, (C_1–C_9) alkyl, (C_1–C_9) alkoxy or phenyl, phenoxy, cyclohexyl, phenylthio, phenylsulfinyl or phenylsulfonyl,

wherein the aforementioned phenyl groups may be unsubstituted or mono-, di- or trisubstituted by halogen, (C_1–C_4)alkoxy or (C_1.C_4)alkoxycarbonyl;

Y is hydrogen, carboxyl, carboxyl protected by a terminal carboxyl protecting group, a carbonyl bonded to the N terminus of a peptide through a peptide bond, (C_1–C_9)alkyl, (C_1–C_9)alkoxy, phenyl phenoxy, cyclohexyl, phenylthio, phenylsulfinyl or phenylsulfonyl wherein the aforementioned phenyl groups may be unsubstituted or mono-, di- or trisubstituted by halogen, (C_1–C_4) alkyl, (C_1-C_4) alkoxy or (C_1.C_4) alkoxycarbonyl; and wherein

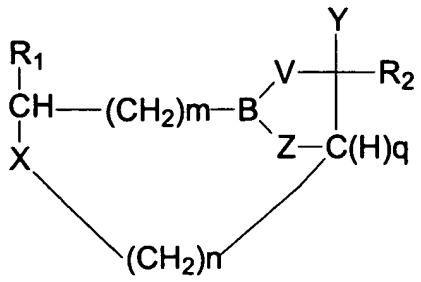
Z is O, CH_2 or NH;

m is 0 or an integer from 1 to 10;

n is 0 or 1; and

q is 1 or 2 provided that if q is 2, then n=0 and there is no bond between X and the carbon bound to Z.

39. A catalytic antibody which catalyzes a chemical reaction of interest and which is elicited through *in vitro* or *in vivo* techniques by an antigen comprising the boron-containing hapten of formula I,



(I)

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wherein

R_1 and R_2 may be the same or different and each is a side chain of a naturally occurring amino acid, a hydroxy containing side chain of a naturally occurring amino acid wherein said hydroxy group may be glycosylated, phosphorylated, sulphonylated or protected by a hydroxy protecting group, a primary amido containing side chain of a naturally occurring amino acid wherein said amido group may be glycosylated, $(C_2–C_4)$ alkyl, $–CH_2CH(CO_2H)_2$, $–(CH_2)_2\ S(O)CH_3$, $–(CH_2)_2\ S(O)_2\ CH_3$, $–(CH_2)_3\ NH_2$ or $–(CH_2)_3\ ONHC(=NH)NH_2$;

V is O, CH_2 or NH;

X is hydrogen, oxygen, amino, amino protected by a terminal amino protecting group, amino bonded to the C terminus of a naturally occurring amino acid to form a peptide bond, amino bonded to the C terminus of a peptide to form a peptide bond, alkene, $(C_1–C_9)$ alkyl, $(C_1–C_9)$ alkoxy or phenyl, phenoxy, cyclohexyl, phenylthio, phenylsulfinyl or phenylsulfonyl, wherein the aforementioned phenyl groups may be unsubstituted or mono-, di- or trisubstituted by halogen, $(C_1–C_4)$ alkoxy or $(C_1.C_4)$ alkoxycarbonyl;

Y is hydrogen, carboxyl, carboxyl protected by a terminal carboxyl protecting group, a carbonyl bonded to the N terminus of a peptide through a peptide bond, $(C_1–C_9)$alkyl, $(C_1–C_9)$alkoxy, phenyl phenoxy, cyclohexyl, phenylthio, phenylsulfinyl or phenylsulfonyl wherein the aforementioned phenyl groups may be unsubstituted or mono-, di- or trisubstituted by halogen, $(C_1–C_4)$alkyl, $(C_1$-$C_4)$alkoxy or $(C_1.C_4)$alkoxycarbonyl; and wherein

Z is O, CH_2 or NH;

m is 0 or an integer from 1 to 10;

n is 0 or 1; and

q is 1 or 2 provided that if q is 2, then n=0 and there is no bond between X and the carbon bound to Z,

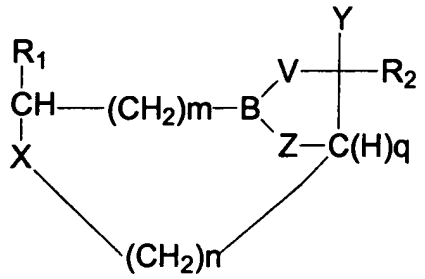
said catalytic antibody having been prepared by a process comprising the steps of:

(a) exposing cells capable of producing antibodies to said antigen and thereby generating antibody producing cells;

(b) hybridizing said antibody producing cells with myeloma cells and thereby generating a plurality of hybridoma cells each producing monoclonal antibodies; and

(c) screening said plurality of monoclonal antibodies to identify a monoclonal antibody which catalyzes said chemical reaction of interest.

42. A method for producing catalytic antibodies which catalyzes a chemical reaction of interest and which are elicited through *in vitro* or *in vivo* techniques by an antigen comprising the boron-containing hapten of formula I,



(I)

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wherein

R_1 and R_2 may be the same or different and each is a side chain of a naturally occurring amino acid, a hydroxy containing side chain of a naturally occurring amino acid wherein said hydroxy group may be glycosylated, phosphorylated, sulphonylated or protected by a hydroxy protecting group, a primary amido containing side chain of a naturally occurring amino acid wherein said amido group may be glycosylated, (C_2–C_4) alkyl, $-CH_2CH(CO_2H)_2$, $-(CH_2)_2\ S(O)CH_3$, $-(CH_2)_2\ S(O)_2\ CH_3$, $-(CH_2)_3\ NH_2$ or $-(CH_2)_3\ ONHC(=NH)NH_2$;

V is O, CH_2 or NH;

X is hydrogen, oxygen, amino, amino protected by a terminal amino protecting group, amino bonded to the C terminus of a naturally occurring amino acid to form a peptide bond, amino bonded to the C terminus of a peptide to form a peptide bond, alkene, (C_1–C_9)alkyl, (C_1–C_9) alkoxy or phenyl, phenoxy, cyclohexyl, phenylthio, phenylsulfinyl or phenylsulfonyl, wherein the aforementioned phenyl groups may be unsubstituted or mono-, di- or trisubstituted by halogen, (C_1–C_4)alkoxy or (C_1-C_4)alkoxycarbonyl;

Y is hydrogen, carboxyl, carboxyl protected by a terminal carboxyl protecting group, a carbonyl bonded to the N terminus of a peptide through a peptide bond, (C_1–C_9)alkyl, (C_1–C_9)alkoxy, phenyl phenoxy, cyclohexyl, phenylthio, phenylsulfinyl or phenylsulfonyl wherein the aforementioned phenyl groups may be unsubstituted or mono-, di- or trisubstituted by halogen, (C_1–C_4)alkyl, (C_1-C_4)alkoxy or (C_1-C_4)alkoxycarbonyl; and wherein

Z is O, CH_2 or NH;

m is 0 or an integer from 1 to 10;

n is 0 or 1; and

q is 1 or 2 provided that if q is 2, then n=0 and there is no bond between X and the carbon bound to Z,

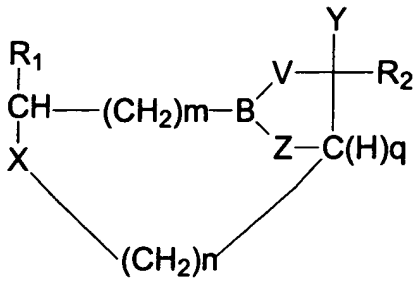
wherein said method comprises the steps of:

(a) exposing cells capable of producing antibodies to said antigen and thereby generating antibody producing cells;

(b) hybridizing said antibody producing cells with myeloma cells and thereby generating a plurality of hybridoma cells each producing monoclonal antibodies; and

(c) screening said plurality of monoclonal antibodies to identify a monoclonal antibody which catalyzes said chemical reaction of interest.

45. A method for catalyzing the cleavage or formation of a peptide linkage or an ester bond in a molecule comprising contacting said molecule with an effective amount of a catalytic antibody elicited by an antigen comprising the boron-containing hapten of formula I,



(I)

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wherein

R_1 and R_2 may be the same or different and each is a side chain of a naturally occurring amino acid, a hydroxy containing side chain of a naturally occurring amino acid wherein said hydroxy group may be glycosylated, phosphorylated, sulphonylated or protected by a hydroxy protecting group, a primary amido containing side chain of a naturally occurring amino acid wherein said amido group may be glycosylated, $(C_2–C_4)$ alkyl, $–CH_2CH(CO_2H)_2$, $–(CH_2)_2\ S(O)CH_3$, $–(CH_2)_2\ S(O)_2\ CH_3$, $–(CH_2)_3\ NH_2$ or $–(CH_2)_3\ ONHC(=NH)NH_2$;

V is O, CH_2 or NH;

X is hydrogen, oxygen, amino, amino protected by a terminal amino protecting group, amino bonded to the C terminus of a naturally occurring amino acid to form a peptide bond, amino bonded to the C terminus of a peptide to form a peptide bond, alkene, $(C_1–C_9)$alkyl, $(C_1–C_9)$ alkoxy or phenyl, phenoxy, cyclohexyl, phenylthio, phenylsulfinyl or phenylsulfonyl, wherein the aforementioned phenyl groups may be unsubstituted or mono-, di- or trisubstituted by halogen, $(C_1–C_4)$alkoxy or $(C_1.C_4)$alkoxycarbonyl;

Y is hydrogen, carboxyl, carboxyl protected by a terminal carboxyl protecting group, a carbonyl bonded to the N terminus of a peptide through a peptide bond, (C_1–C_9)alkyl, (C_1–C_9)alkoxy, phenyl phenoxy, cyclohexyl, phenylthio, phenylsulfinyl or phenylsulfonyl wherein the aforementioned phenyl groups may be unsubstituted or mono-, di- or trisubstituted by halogen, (C_1–C_4)alkyl, (C_1-C_4)alkoxy or (C_1.C_4)alkoxycarbonyl; and wherein

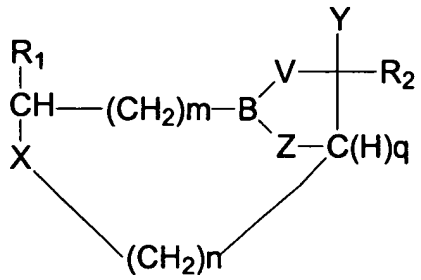
Z is O, CH_2 or NH;

m is 0 or an integer from 1 to 10;

n is 0 or 1; and

q is 1 or 2 provided that if q is 2, then n=0 and there is no bond between X and the carbon bound to Z.

48. A method for catalyzing the cleavage or formation of a specific peptide linkage or an ester bond within a specific amino acid sequence of a molecule which comprises: contacting said molecule with an effective amount of a catalytic antibody elicited with a boron-containing hapten of formula I,



(I)

wherein

R_1 and R_2 may be the same or different and each is a side chain of a naturally occurring amino acid, a hydroxy containing side chain of a naturally occurring amino acid wherein said hydroxy group may be glycosylated, phosphorylated, sulphonylated or protected by a hydroxy

protecting group, a primary amido containing side chain of a naturally occurring amino acid wherein said amido group may be glycosylated, (C_2–C_4) alkyl, –$CH_2CH(CO_2H)_2$, –$(CH_2)_2$ $S(O)CH_3$, –$(CH_2)_2$ $S(O)_2$ CH_3, –$(CH_2)_3$ NH_2 or –$(CH_2)_3$ $ONHC(=NH)NH_2$;

V is O, CH_2 or NH;

X is hydrogen, oxygen, amino, amino protected by a terminal amino protecting group, amino bonded to the C terminus of a naturally occurring amino acid to form a peptide bond, amino bonded to the C terminus of a peptide to form a peptide bond, alkene, (C_1–C_9)alkyl, (C_1–C_9) alkoxy or phenyl, phenoxy, cyclohexyl, phenylthio, phenylsulfinyl or phenylsulfonyl, wherein the aforementioned phenyl groups may be unsubstituted or mono-, di- or trisubstituted by halogen, (C_1–C_4)alkoxy or (C_1.C_4)alkoxycarbonyl;

Y is hydrogen, carboxyl, carboxyl protected by a terminal carboxyl protecting group, a carbonyl bonded to the N terminus of a peptide through a peptide bond, (C_1–C_9)alkyl, (C_1–C_9)alkoxy, phenyl phenoxy, cyclohexyl, phenylthio, phenylsulfinyl or phenylsulfonyl wherein the aforementioned phenyl groups may be unsubstituted or mono-, di- or trisubstituted by halogen, (C_1–C_4)alkyl, (C_1-C_4)alkoxy or (C_1.C_4)alkoxycarbonyl; and wherein

Z is O, CH_2 or NH;

m is 0 or an integer from 1 to 10;

n is 0 or 1; and

q is 1 or 2 provided that if q is 2, then n=0 and there is no bond between X and the carbon bound to Z,

said hapten being homologous to said specific amino acid sequence.